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CONTENTS

Editorial	289
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DOSSIER: CIRCULATION OF ANTIBIOTICS: HISTORICAL RECONSTRUCTIONS

Guest editors: María Jesús Santesmases and Christoph Gradmann

Circulation of antibiotics: an introduction

María Jesús Santesmases and Christoph Gradmann.....	293
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Magic bullets and moving targets: antibiotic resistance and experimental chemotherapy, 1900-1940

Christoph Gradmann	305
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1.—Histories of antibiotic resistance. 2.—A therapy with side effects. 3.—The impact of resistance. 4.—A «wholly mysterious phenomenon». 5.—A revival. 6.—Conclusions.

ABSTRACT: It was in the 1940s that antibiotic resistance arose as an object of study for clinical medicine. Somewhat earlier it had become an important analytical tool for bacterial geneticists. However, the concept of antibiotic resistance as an induced and inheritable trait of microbial species was introduced a generation earlier in the years preceding the First World War.

The paper reconstructs the concept that was put forward by the German immunologist Paul Ehrlich in 1907. He came across the phenomenon when trying to develop chemotherapies for trypanosomiasis, the best known of which is African sleeping sickness. However, resistance was studied by him

for other than therapy-related purposes. It provided a productive laboratory model for the study of cell functions. Induced resistance to chemicals facilitated the development of ideas on the relation of a parasite's cellular metabolism and of drug action, i.e. by providing a negative proof for the presence of chemoreceptors on the surfaces of parasite cells.

This approach also serves to explain why British and German researchers continued to study the phenomenon of induced resistance in microbes for decades —despite it being absent from clinical medicine. After all, there existed very few chemotherapies of infectious diseases prior to the arrival of the sulfa drugs. Moreover, resistance to these medicines was rarely observed. However, being part and parcel of Ehrlich's theories, his views on resistance were also criticised together with these. It was in particular Henry Dale who would challenge Ehrlich's views of resistance as an inheritable and stable trait of microbes. Instead, he insisted that understanding this «wholly mysterious phenomenon» required taking into account some host interaction. Induced resistance, which had come into being as a chance discovery in the chemotherapy of sleeping sickness, thus became one of the more important laboratory models of 20th-century immunological research. Its early history is largely discontinuous with later work, and antimicrobial resistance as it evolved from 1900 to 1940 followed other trajectories than those which became relevant after 1940.

Innovators, deep fermentation and antibiotics: promoting applied science before and after the Second World War

Robert Bud. 323

1.—Introduction. 2.—Know-how and deep-fermentation. 3.—Wartime. 4.—Post-war. 5.—Conclusion: on the disappearance of stories.

ABSTRACT: It was in the 1940s that antibiotic resistance arose as an object of study for clinical medicine. Somewhat earlier it had become an important analytical tool for bacterial geneticists. However, the concept of antibiotic resistance as an induced and inheritable trait of microbial species was introduced a generation earlier in the years preceding the First World War. The paper reconstructs the concept that was put forward by the German immunologist Paul Ehrlich in 1907. He came across the phenomenon when trying to develop chemotherapies for trypanosomiasis, the best known of which is African sleeping sickness. However, resistance was studied by him for other than therapy-related purposes. It provided a productive laboratory model for the study of cell functions. Induced resistance to chemicals facilitated the development of ideas on the relation of a parasite's cellular metabolism and of drug action, i.e. by providing a negative proof for the existence of chemoreceptors on the surfaces of parasite cells. This approach does also serve to explain why British and German researchers continued to study the phenomenon of induced resistance in microbes for decades —despite it being absent from clinical medicine. After all, there existed very few chemotherapies of infectious diseases prior to the arrival of the sulfa drugs. Moreover, resistance to such medicines was rarely observed. However, being part and parcel of Ehrlich's theories, his views

on resistance were also criticised together with these. It was in particular Henry Dale who would challenge Ehrlich's views of resistance being an inheritable and stable trait of microbes. Instead he insisted that understanding this «wholly mysterious phenomenon» required taking into account some host interaction. Induced resistance, which had come into being as a chance discovery on the chemotherapy of sleeping sickness, thus became one of the more important laboratory models of twentieth-century immunological research. Its early history is largely discontinuous with later work, and antimicrobial resistance as it evolved from 1900 to 1940 followed other trajectories than those which became relevant after 1940.

«A Chain is gonna come». Building a penicillin production plant in post-war Italy

Mauro Capocci 343

1.—The *Istituto Superiore di Sanità*. 2.—UNRRA plant and chain's penicillin. 3.—The ISS between business and politics. 4.—Conclusion.

ABSTRACT: In 1947, Ernst Chain moved from Oxford to Rome, hired as head of a new biochemistry department and of a penicillin production pilot plant in the *Istituto Superiore di Sanità* (Higher Health Institute). Here, he managed to make Rome one of the most important centres in the international network of antibiotic science. However, the development of the state-operated centre was not easy. Political and economic pressures, exerted from both home and abroad, posed many obstacles to the plan devised by Domenico Marotta, the Director General of the Institute. The paper reconstructs Chain's venture in Rome, which lasted until 1964, while framing the history of the penicillin production plant in the context of diplomatic negotiations, national politics, and science policies.

Regulation and the circulation of knowledge: penicillin patents in Spain

Ana Romero de Pablos 363

1.—Introduction. 2.—Patent archives as sources for historical reconstruction. 3.—The Spanish dictatorship and the autarchy. 4.—Patents as regulators. 5.—Foreign competition. 6.—Regulation and the circulation of knowledge. 7.—Conclusions: liability and predictability.

ABSTRACT: This paper tells the early history of penicillin patenting in Spain. Patents turn out to be useful instruments for analysing the management of knowledge and its circulation in different professional and geographical domains. They protected knowledge while contributing to standardisation. Patents also ensured quality and guaranteed reliability in manufacturing, delivering and prescribing new drugs. They gained special prominence by allowing the creation of a network in which politics, economics, business, industrial power, public health and international cooperation fields came together. The main source of information used for this purpose has been the earliest patent applications for penicillin in Spain between 1948 and 1950, which

are kept in the Historical Archives of the *Oficina Española de Patentes y Marcas*. The study of these patents for penicillin shows their role as agents in introducing this drug into Spain.

Negotiating hospital infections: the debate between ecological balance and eradication strategies in British hospitals, 1947-1969

Flurin Condrau and Robert G. W. Kirk 385

1.—Introduction. 2.—From the hospital environment to the healthy carrier. 3.—Conceptualising the control of hospital infections 4.—Conclusion.

ABSTRACT: This paper reviews and contrasts two strategies of infection control that emerged in response to the growing use of antibiotics within British hospitals, c.1946-1969. At this time, we argue, the hospital became an arena within which representatives of the medical sciences and clinical practices contested not so much the content of knowledge but the way that knowledge translated into practice. Key to our story are the conceptual assumptions about antibiotics put forward by clinicians, on the one hand, and microbiologists on the other. The former embraced antibiotics as the latest weapon in their fight to eradicate disease. For clinicians, the use of antibiotics were utilised within a conceptual frame that prioritised the value of the individual patient before them. Microbiologists, in contrast, understood antibiotics quite differently. They adopted a complex understanding of the way antibiotics functioned within the hospital environment that emphasised the relational and ecological aspects of their use. Despite their broader environmental focus, microbiologists focussed on the ways in which bacteria travelled led to ever greater emphasis being placed on the «healthy» body which, having been exposed to antibiotics, became a dangerous carrier of resistant staphylococcal strains. The surrounding debate regarding the appropriate use of antibiotics reveals the complex relationship between hospital, the medical sciences and clinical practice. We conclude that the history of hospital infections invites a more fundamental reflection on global hospital cultures, antibiotic prescription practices, and the fostering of an interdisciplinary spirit among the professional groups living and working in the hospital.

Screening antibiotics: industrial research by CEPA and Merck in the 1950s

María Jesús Santesmases 407

1. —Introduction. 2.—The factory system and industrialised research. 3.—Selman Waksman's research agenda. 4.—Industrial connection. 5.—Setting tasks for «screening». 6.—Screening research patterns. 7.—Research in the factory. 8. —At work. 9.—Concluding remarks.

ABSTRACT: This article is an account of a screening programme in search of new antibiotics established by CEPA (Compañía Española de Penicilinas y Antibióticos) and Merck in Madrid in 1954. An exploration of the genealogy for such a programme, its narratives and practices, shows that the main inspiration

for this programme was the factory system of production, on the one hand, and Selman Waksman's research agenda on microorganisms of the soil, on the other. In this article, the relationship between industrial production of antibiotics and the research programme aimed at identifying new candidate drugs is examined. I suggest that this screening programme in search of new antibiotics was organised like industrial manufacturing. The research objects and tools came, both materially and conceptually, from industrial production: a line of artisanship put together in order to obtain a product with the collaboration of every member of the production line. Following the style developed by Selman Waksman in Rutgers, the screening programme evaluated samples manually, and microbiological skills were enhanced with every test. The Madrid team's practice of applying instructions for use led to the circulation of knowledge and practices, including research material and microbiological methods.

ARTICLES

The evolution of height in France and Spain, 1770-2000.

Historiographic background and new evidence

José Miguel Martínez Carrión and Javier Puche Gil 429

1.—Introduction 2.—The development of anthropometry in France 3.—The Spanish replica 4.—The birth of auxology and its influence on historiography. 5.—Evolution of the height of men in France and Spain, a comparative perspective. 6.—Conclusions.

ABSTRACT: Height is used by paediatricians and anthropologists as a measure of the health and well-being of human populations. Over the past few decades, it has been used by historians as an indicator of the biological standard of living in studies on the impact of environmental, social and economic transformations on well-being in the past. This article describes the historical contributions made by different specialists on this issue and compares the evolution of the height of men in France and Spain. Annual military recruitment data from the 1770s until the end of the 20th century show a secular trend in both countries and reveal cycles that result from periods of deterioration in health and nutritional status.

Medicine of the passions in 19th century Spain

Enric J. Novella 453

1.—Introduction. 2.—Physiology of the passions. 3.—Medicine and morality. 4.—From passions to emotions.

ABSTRACT: This article explores the important place occupied by the passions in the theoretical discourses and professional rhetoric of 19th century Spanish medicine. In order to expand their explanatory and therapeutic resources and, above all, to endorse their competence as experts in the study and management of the passions, Spanish physicians adopted and promulgated a number of postulates in this regard, including the relevance of physiological research, and

the importance of pathogenic effects, social risks, clinical semiology, differential diagnosis and therapy. These not only laid the conceptual foundations for emerging disciplines and practices such as psychiatry, hygiene and moral therapy, but can also be seen, in retrospect, as anticipating central assumptions of modern sciences of the mind. However, this medicalisation of the passions led them to be gradually discredited in favour of the concept of the emotions (allegedly more physiological and lacking moral connotations and therefore more objective). By the end of the 19th century, the passions had almost disappeared from scientific discourses on affectivity and the psyche.

How patients built up the practice of the lay homeopath Clemens von Bönninghausen. Quantitative and qualitative aspects of patient history

Marion Baschin 475

1.—Introduction. 2.—The homeopath and his journals. 3.—The practice. 4.—The patients. 5.—The illnesses. 6.—Conclusions.

ABSTRACT: Statistics seem to give little information about individuals' fates. The interwoven connections between quantitative and qualitative aspects of historical research work can be elucidated with the help of patient journals. We focus on the patients who, between 1829 and 1864, built up the practice of the lay homeopath Clemens Maria Franz von Bönninghausen in Münster, Westphalia. Questions of practice, the social structure of the clientele and the diseases Bönninghausen treated are also considered.

«The duty to improve»: working-class hygiene and identity in socialism in Madrid

Ricardo Campos 497

1.—Introduction. 2.—Social inequality and disease in the socialist discourse. 3.—Hygiene, an instrument promoting workers' dignity. 4.—Conclusion.

ABSTRACT: This study analyzes socialist discourse and demands on health policies between 1883 and 1904 with the aim of demonstrating the high degree of politicization of this discourse and the desire for social and political integration. It also analyzes the political role played by health and hygiene in the construction of a working-class identity and the ideological tensions and ambiguities produced by the need to take on the discourse of others, i.e., scientists. However, this was necessary to formulate demands in pursuit of the social inclusion of workers as citizens with full citizens' rights, promoting their dignity.

The place of cancer in Portuguese health statistics

Rui Manuel Pinto Costa 527

1.—A rare or rarely diagnosed disease? 2.—Hygienism and health policy: origin of statistical deficiencies. 3.—Awakening of a new scourge. 4.—Azevedo Neves

and the Report of 1904. 3.2.—Political intervention and the imperative of the fight against cancer 4.—Portuguese Institute of Oncology and the evolution of statistics and the true place of cancer. 5.—Final considerations.

ABSTRACT: This study aims to show the influence of statistical studies on the establishment of the fight against cancer in Portugal. Cancer visibility became more important due to statistic analyses, which took the form of reports in Portugal and were not always complete and frequently distant from reality. Although the impact of these reports was not felt immediately, they led over the medium-term to the establishment of the Portuguese Institute of Oncology, created in 1923 based on international models. New data obtained by the Institute allowed the correction of important errors in relation to the true presence of cancer in Portuguese health statistics in the 1930.

REVIEWS

- Richard Cleminson. Anarquismo y sexualidad (España, 1900-1939)**
Ramón Castejón Bolea 553
- María Ángeles Delgado Martínez, ed. Margalida Comas Camps (1892-1972) científica i pedagoga**
Esther Rubio Herráez 557
- Francisco J. Martínez Antonio. Intimididades de Marruecos. Miradas y reflexiones de médicos españoles sobre la realidad marroquí a finales del siglo XIX**
Álvaro Girón Sierra 559
- Ellen S. More, Elizabeth Fee, Manon Parry, eds. Women physicians and the cultures of medicine**
Lorena Saletti Cuesta 564
- Warwick Anderson. The collectors of lost souls: Turning Kuru scientists into whitemen**
Antonio M. Ortega Martos 568
- Mari Luz Esteban; Josep M. Comelles; Carmen Díez Mintegui, eds. Antropología, género, salud y atención**
Nuria Romo 572

Samuel Auguste Tissot. De la médecine civile ou de la police de la médecine

María Isabel Porras Gallo 574

William Gallois. The administration of sickness. Medicine and ethics in nineteenth-century Algeria

Francisco Javier Martínez Antonio 577

BOOKS RECEIVED 583

GUIDELINES FOR SUBMISSION OF ORIGINAL PAPERS 589